Darwin's illness: Chagas' disease resurgens[1]

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The centenary of Charles Robert Darwin's death in 1982 brought forth a spate of celebrations and publications paying tribute to one of science's foremost immortals. Many have speculated on the nature of Darwin's drawn-out illness (e.g. Alvarez 1959, Pickering 1974). On the centenary of 'The Origin of the Species' (24 November 1859), Adler (1959) suggested Chagas' disease (South American trypanosomiasis); it was also the 50th anniversary of the description by Chagas (1909) of the *Triatoma infestans* vector and the *Trypanosoma cruzi* agent. During the voyage of the *Beagle* Darwin studied the Triatoma Reduviidae for 4 months in Chile, and suffered a severe illness in September-October 1834 on returning to Valparaiso from the interior. This seven-week illness has been attributed to typhoid (Keith 1955), but there are no recorded details and other members of the land party were not involved. Later, Darwin described a specific incident on 25 March 1835, after crossing the high Andes from Valparaiso to Luxan, Argentine, where he was bitten by Reduviid bugs. Subsequently, Woodruff (1965) examined his fellow parasitologist's proposition – only to reject it.

Chagas' disease, which affects 7–10 million people in the Americas, has been intensively studied recently (World Health Organization 1960, Santos-Buch 1979). Prophylactic immunization (Teixeira 1979) or improvement in social conditions rather than chemotherapy (Avila & Avila 1981) may be more effective in reducing its incidence. Clinically, an active reactive phase is followed by a latency up to 20 years. This results from a brisk intracellular multiplication of *T. cruzi* organisms, eventually checked but not eradicated by host immune responses. The early infective process may thus be essentially clinically silent (Santos-Buch 1979, Teixeira 1979), or an explosive reaction with a proportion of deaths. Some 10% of those recovering from the initial acute phase develop chronic cardiac and gastrointestinal symptoms. Prominent effects are myocardial destruction, and mega-colon and mega-oesophagus, attributable to antigen-antibody reactions with destruction of neurones and muscle cells of cardiac and skeletal muscle and smooth muscle of the gastrointestinal tract. The time sequence of symptoms accords better with an immune disorder (Santos-Buch 1979, Brener 1980, Kagan 1980) than an acute-chronic infective process. The immunological processes identified control parasitaemia on the one hand, and promote extensive peripheral nerve and cardiac muscle degeneration on the other. The recent isolation of a monoclonal antibody raised against rat dorsal root ganglia that is cytotoxic only to mammalian neurones susceptible in Chagas' disease, and also labels *T. cruzi*, implicates an autoimmune reaction (Wood *et al.* 1982); myocardial cells also appear to be subject to a similar autoimmune process (Brener 1980, Kagan 1980). A further effector mechanism that may explain many of the pathological findings is granulocyte cytotoxicity (Lopez *et al.* 1983). Death in the chronic stage commonly occurs from heart failure, cardiac dysrhythmias or block.

In the case of Darwin, there is some evidence for the acute stage (1834–35). From 1835 to 1841, Darwin reported no illness (latent phase). During the years 1841–65, Darwin complained incessantly in his conversations and correspondence of palpitations, lassitude and 'sense of extreme fatigue', accompanied at times by trembling, flatulence and vomiting; 'my confounded stomach' and 'poor dyspeptic'. Darwin conducted a most voluminous correspondence (Darwin 1887, Darwin & Seward 1903). In his letters to botanists Joseph

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Hooker, Hugh Falconer and Asa Gray, naturalists Alfred Wallace and Henry Bates, geologist Charles Lyell, Thomas Huxley and others, from the mid-1840s to late 1860s, there are frequent references to 'very indifferent health', 'never comfortable for 48 hours', 'violent vomiting and trembling', 'Never pass a day without much discomfort and the sense of extreme fatigue', 'vomiting every day for eleven days', etc., but virtually nothing on this score thereafter. No doctor, including eminent and astute physicians such as Sir Alexander Clark, Brinton and Bence-Jones, discoverer of 'a new substance occurring in the urine of a patient with Mollities Ossium' (Bence-Jones 1848), found any physical signs over a period of 30 years. Further, Darwin, in his 1851–55 health diary – a daily record of his symptoms (Bernstein 1982) – does not note the taking of any medication. Periodicity of symptoms occurred, with reported episodes of some severity noted for 1840–41, 1848–52 and 1863–65.

But in his prolific writing years (1866–82), Darwin enjoyed reasonable, even good, health. His son Francis noted that 'during the last years of his life the state of his health was a cause of satisfaction and hope to his family . . . he suffered less distress and discomfort, and was able to work more steadily' (Darwin 1887, vol 3, p 355). This was, possibly, an asymptomatic or quiescent chronic disease process and continued until four months before his death, when Darwin suffered the first of several heart attacks, culminating in the fatal episode of 19 April 1882. This chronological analysis of Darwin's 'illness' accords better with the objective and time-table aspects of Darwin's scientific experiments and writings than the oft-claimed biographic assertions of 40 years' ill-health.

It is of interest to note that the first identified human case of South American trypanosomiasis (Chagas 1916) was in a 2-year-old girl, Berenice, who when re-examined in 1961 (age 53 years) exhibited no clinical symptoms but was a carrier of Chagas' disease (Salgado *et al.* 1963). In 1980, Berenice still evidenced a positive complement fixation test, and parasites were also cultured from her blood by xenodiagnosis (Lewinsohn 1981). But, like Darwin, her clinical examination was entirely normal, and no cardiac, digestive or other manifestations of chronic Chagas' disease could be found. She died in June 1981 (age 73 years), apparently due to heart disease, but whether from Chagasic cardiomyopathy is still under investigation (Lewinsohn 1982).

Whether Darwin was infected with *T. cruzi* is only a possibility. While the sequence of his complaints is consistent with the immune time processes of Chagas' disease, this diagnosis still and probably always will, in the absence of immunological and objective investigations involving the heart and hollow abdominal viscera, remain speculative.

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